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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/089,894      06/03/98      BOMSHTEYN      A      19603/871 (CR)

HM12/0810

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EXAMINER

LUKTON, D

ART UNIT

PAPER NUMBER

1653

DATE MAILED:

08/10/01

*18*

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
09/089,894

Applicant(s)

Bomshyeyn

Examiner

David Lukton

Art Unit

1653



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1) ☒ Responsive to communication(s) filed on May 29, 2001

2a) ☐ This action is FINAL.

2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 1-47 is/are pending in the application

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration

5) ☒ Claim(s) 1 and 2 is/are allowed

6) ☒ Claim(s) 3-47 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirements

## Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some\* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_

20) ☐ Other: \_\_\_\_\_

Pursuant to the directives of paper No. 16 (filed 5/29/01), claims 13, 15, 25, 27 have been amended. Claims 1-47 remain pending.

Applicants' arguments filed 5/29/01 have been considered and found persuasive in part.

\*

Claims 3-47 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 3 is indefinite with respect to the process steps, particularly with regard to the isolation of the final product. If the final product is never isolated, how can it be used? The following is suggested (the designations "formula II" and "formula III" have been created here):

*A method of synthesizing a diether of formula II*  
*{structure as recited}*  
*wherein R is alkyl,*

*said method comprising*

*(a) reacting a di-alcohol of formula III with a nitrile of formula  $RC \equiv N$  for a time and under conditions effective to form the diether of formula II, and*

*(b) isolating the diether of formula II.*

- Each of claims 7, 10 and 11 is indefinite with respect to the process steps, particularly with regard to the isolation of the final product. If the final product is never isolated, how can it be used? It is suggested that a step be added to recite isolation of the final product.
- Claim 10 is broader than claim 7. Either the scope of claim 7 should be expanded

to include the steps recited in claim 7, or else claim 10 should be made independent. The same applies with respect to the relationship between claims 10 and 11.

- Each of claims 14, 16, 19, 21, 26, 28 recite the phrase "SEQ. ID. No.".

This should instead be: **SEQ ID NO:**

- Claim 17 is indefinite as to the requirement for isolation of the final product. In addition, the claim recites "converting the betulinol peptide with an antibody", thus rendering the claim indefinite. The following is suggested (support for "peptide bond-forming reagent" can be rationalized based on the text present on p. 18, line 4):

*A method of producing a betulinol antibody conjugate of formula (V)  
{formula as recited}*

*wherein Y is ...*

*said method comprising*

*(a) reacting a betulinol peptide of formula (VI) with an antibody in the presence of a peptide bond-forming reagent for a time and under conditions effective to form a peptide bond between a carboxyl group on the peptide moiety of formula (VI) and an amino group on the antibody, and*

*(b) isolating the betulinol antibody conjugate of formula (V).*

- Claim 22 recites "wherein, said providing the betulinol peptide comprises". However, claim 22 pertains to more than mere "providing"; it is a reaction. One option would be to write claim 22 in independent form. Another option is to recite the following (this process is briefly discussed on p. 18, line 18+):

*A method according to claim 17 wherein the betulinol peptide of formula (VI) is obtained by a process comprising*

*(a) reacting a compound of formula (VII) with a peptide of the formula  
H-peptide-OH*

*in the presence of a suitable catalyst for a time and under conditions effective to form a covalent bond between the amino terminus of the peptide and the betulinol*

*hydroxyl group, and*

*(b) isolating the betulino<sup>1</sup> peptide of formula (VI).*

The same issues apply in claims 29-31, 34, 35 as in claim 22.

- Claim 23 is indefinite as to the requirement for isolation of the final product. In addition, the claim recites "converting the haloacetylhydrazide with an antibody", thus rendering the claim indefinite. The following is suggested:

*A method of producing a betulinol antibody conjugate of formula (VIII)*

*{formula as recited}*

*wherein Y is ...*

*said method comprising*

*(a) reacting a haloacetylhydrazide of formula (IX) with an antibody for a time and under conditions effective to form a covalent bond between the -NHNHCOCH<sub>2</sub>- moiety of formula (IX) and an amino group on the antibody, and*

*(b) isolating the betulinol antibody conjugate of formula (VIII).*

- Claim 29 recites the term "p-nitrophenyl haloacetate". Either of the following would be better:

reacting the hydrazide with *para*-nitrophenyl  $\alpha$ -haloacetate...

- or -

reacting the hydrazide with the *para*-nitrophenyl ester of an  $\alpha$ -haloacetic acid...

- In claim 36, to the left of the structure is the word "an". What is the purpose of this?
- Claim 32 recites: "wherein A are independently selected". Either of the following would be better:

*wherein each "A" moiety is independently selected*

*wherein each "A" substituent is independently selected*

- Claim 32 recites: “independently selected from a CHO group **or** a moiety...”. However, use of the conjunction “or” in this situation constitutes improper Markush format.
- Claim 33 is rendered indefinite because of the failure to recite isolation of the final product.
- Claim 33 recites (last several lines, page 46):

“said method comprising:  
providing a carrier molecule having the formula:

...  
converting the carrier molecule with a hydrazide having the formula”

However, this is somewhat indefinite with regard to the process steps. The following is suggested:

*said method comprising*

*(a) reacting a carrier molecule of formula XVII with a hydrazide of formula XVIII for a time and conditions effective to form a hydrazone adduct;*

*(b) reacting the hydrazone adduct of step (a) with with an antibody in the presence of a peptide bond-forming reagent for a time and under conditions effective to form a peptide bond between the carboxyl group of the C-terminal glycine of the hydrazone adduct and an an amino group on the antibody; and*

*(c) isolating the betulinol-antibody conjugate of formula XV.*

- In claims 38-39, 45, 46 the term “spacer” should be in quotation marks, to distinguish its status as a substituent variable from the more general meaning of the term.
- Claim 41 is rendered indefinite as to process steps, for example, isolation of the product. In addition, the relationship between the spacer and the crosslinker is not made clear.

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- Claim 32, line 2 recites "are independently". The singular of "are" should be used, since it is referring to "each".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton. Phone: (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



DAVID LUKTON  
PATENT EXAMINER  
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